Information Disclosure Statement

1. The information disclosure statement filed May 19, 2009 fails to comply with 37 CFR 1.97(d) because it lacks a statement as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered.

2. Additionally, the listing of references appears to have been previously submitted August 17, 2006.

EXAMINER'S AMENDMENT

3. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Dean G Stathakis, Ph.D, Registration Number 54,465 on May 28, 2009.

The application has been amended as follows:

4. In light of claim 1 being a generic claim, withdrawn claims 3, 9-15 and 23-25, are herein rejoined in light of 37 CFR 1.141. The allowance of a generic claim, entitles applicant to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

5. Claim 1 is directed to an allowable generic method. Because all claims previously withdrawn from consideration under 37 CFR 1.141 have been rejoined, **the election of species**

requirement as set forth in the Office action mailed on June 20, 2008 is hereby withdrawn. In view of the withdrawal of the election of species requirement as to the rejoined species of inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Please cancel claim 2.

Please Amend Claim 1 as follows:

Claim 1. (Amended) A method of detecting Botulinum toxin serotype A (BoNT/A) activity in a sample, the method comprising the steps of:

a) contacting a sample to a cell that contains an exogenous Fibroblast Growth Factor Receptor 3 (FGFR3) and an endogenous synaptosome-associated protein of 25000 Daltons (SNAP-25) ,wherein said cell is genetically engineered to express a nucleic acid molecule encoding said FGFR3; and wherein said cell is capable of BoNT/A intoxication; and

b) detecting the presence of BoNT/A activity of said cell relative to a control cell~~, where~~ by detecting the presence of endogenous SNAP-25 cleavage product from said cell ~~is indicative of BoNT/A activity~~.

6. The following is an examiner's statement of reasons for allowance:

While the prior art of record discloses cell based assays of detecting serotype A botulinum toxin based upon SNAP-25 cleavage product, the prior art is silent with respect to genetically engineered cells that express a nucleic acid molecule that encodes Fibroblast Growth Factor Receptor 3 to which the botulinum toxin type A binds.

The prior art cell based assays were functional assays, that did not know what receptor, nor the nucleic acid that encodes the receptor to which botulinum toxin type A bound in order to be internalized into the cell resulting in cleavage of SNAP-25 and generation of SNAP-25 cleavage product. So while an inherency rejection for a cell based assay was made of record over the naturally occurring receptor, the identity, nature and coding sequence for botulinum toxin type A receptor was not known at the time of filing of the instant Application.

Additionally, while Onose et al recombinantly expressed FGFR3 in a papillary thyroid carcinoma cell line (abstract), the reference is silent with respect to botulinum toxin binding to this receptor. Nemoz-Gaillard et al is being made of record to show that SNAP-25 is not predictably expressed in all carcinomas from a common body region, and only one medullary thyroid cell line CA77 is known to express SNAP-25 endogenously(see Figure 1). A medullary thyroid carcinoma is a rare type of thyroid carcinoma, and is different from the more common type of papillary thyroid carcinoma used by Onose et al for recombinant expression of FGFR3; the papillary carcinoma cell lines of Onose et al do not express SNAP-25 and would not be obvious cell lines for use in the instantly claimed method.

The prior art of record does not teach nor reasonably suggest that botulinum toxin binds to FGFR3, nor suggest the use of a genetically engineered cell expressing FGFR3 in a bioassay to measure botulinum neurotoxin type A activity by measuring proteolytic SNAP-25 cleavage product.

The instantly claimed method that utilizes a genetically engineered cell that genetically engineered/expressed Fibroblast Growth Factor Receptor 3 in a cell that naturally expresses SNAP-25 defines a method that is not taught, nor reasonably suggested in the prior art of record, thus defining allowable subject matter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645

/Ginny Portner/
Examiner, Art Unit 1645
May 28, 2009